

This listing of claims will replace all prior versions, and listings, of claims in the application.

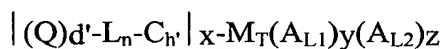
Listing of Claims:

1-19. (canceled)

20. (currently amended) ~~The method of Claim 17~~ A method for imaging a pulmonary embolus comprising the steps of:

- a. localizing a radiolabelled compound at the pulmonary embolus;
- b. acquiring image slices representing the concentration of radioactivity within the radiolabelled pulmonary embolus;
- c. assembling the image slices into a three-dimensional matrix of data;
- d. scanning the three-dimensional matrix of data along an array of parallel lines to determine a maximum value along each line; and
- e. assigning the maximum value along each line to a pixel in a two-dimensional array, the position of the pixel corresponding to the position of the line in the array of parallel lines;

wherein the localization step comprises the step of localizing a compound of the formula (I), and pharmaceutically acceptable salts thereof, at the ~~thrombus~~ pulmonary embolus:



(I) ,

wherein,

Q is a glycoprotein IIb/IIIa binding compound;

d' is 1 - 20;

L_n is a linking group of formula:

M¹-[Y¹(CR⁵⁵R⁵⁶)_f(Z¹)_{f'}Y²]_f-M²,

wherein:

M¹ is -[(CH₂)_gZ¹]_{g'}-(CR⁵⁵R⁵⁶)_{g''}-;

M² is -(CR⁵⁵R⁵⁶)_{g''}-[Z¹(CH₂)_g]_{g'}-;

g is ~~0~~independently 0-10;

g' is ~~0~~independently 0-1;

g'' is ~~0~~independently 0-10;

f is ~~0~~independently 0-10;

f' is independently 0-10;

f'' is independently 0-1;

~~Y¹ and Y², are independently selected at each occurrence from: a bond, O, NR⁵⁶,~~

~~C=O, C(=O)O, OC(=O)O, C(=O)NH, C=NR⁵⁶, S, SO, SO₂, SO₃, NHC(=O), (NH)₂C(=O),~~
and (NH)₂C=S;

Y¹ is a bond;

Y² is NHC(=O);

Z^1 is independently selected at each occurrence from a C₆-C₁₄ saturated, partially saturated, or aromatic carbocyclic ring system, substituted with 0-4 R^{57} ; and a heterocyclic ring system, substituted with 0-4 R^{57} ;

R^{55} and R^{56} are independently selected at each occurrence from: hydrogen; C₁-C₁₀ alkyl substituted with 0-5 R^{57} ; and alkaryl wherein the aryl is substituted with 0-5 R^{57} ;

R^{57} is independently selected at each occurrence from the group: hydrogen, OH, NHR^{58} , $C(=O)R^{58}$, $OC(=O)R^{58}$, $OC(=O)OR^{58}$, $C(=O)OR^{58}$, $C(=O)NR^{58}$, $C\equiv N$, SR^{58} , SOR^{58} , SO_2R^{58} , $NHC(=O)R^{58}$, $NHC(=O)NHR^{58}$, $NHC(=S)NHR^{58}$; or, alternatively, when attached to an additional molecule Q, R^{57} is independently selected at each occurrence from the group: O, NR^{58} , C=O, $C(=O)O$, $OC(=O)O$, $C(=O)N-$, $C=NR^{58}$, S, SO, SO₂, SO₃, $NHC(=O)$, $(NH)_2C(=O)$, $(NH)_2C=S$; and,

R^{58} is independently selected at each occurrence from the group: hydrogen; C₁-C₆ alkyl; benzyl, and phenyl;

M_T is a transition metal radionuclide;

C_h is a radionuclide metal chelator or bonding unit bound to the transition metal radionuclide of the formula $R^{40}R^{41}N=N$, $R^{40}N$, or $R^{40}N=N(H)$ selected from the group consisting of: $R^{40}N=N$, $R^{40}R^{41}N=N$, $R^{40}N$, or $R^{40}N=N(H)$;

R^{40} is a heterocycle substituted with 1 R^{52} independently selected at each occurrence from the group: a bond to L_n , C1-C10 alkyl substituted with 0-3 R^{52} , aryl substituted with 0-3 R^{52} , cycloalkyl substituted with 0-3 R^{52} , heterocycle substituted with 0-3 R^{52} , heterocycloalkyl substituted with 0-3 R^{52} , aralkyl substituted with 0-3 R^{52} and alkaryl substituted with 0-3 R^{52} ;

R^{41} is independently selected from the group: hydrogen, aryl substituted with 0-3 R^{52} , C1-C10 alkyl substituted with 0-3 R^{52} , and a heterocycle substituted with 0-3 R^{52} ;

R^{52} is independently selected at each occurrence from the group: a bond to L_n , $=O$, F, Cl, Br, I, CF_3 , CN, CO_2R^{53} , $C(=O)R^{53}$, $C(=O)N(R^{53})_2$, CHO, CH_2OR^{53} , $OC(=O)R^{53}$, $OC(=O)OR^{53a}$, OR^{53} , $OC(=O)N(R^{53})_2$, $NR^{53}C(=O)R^{53}$, $NR^{54}C(=O)OR^{53a}$, $NR^{53}C(=O)N(R^{53})_2$, $NR^{54}SO_2N(R^{53})_2$, $NR^{54}SO_2R^{53a}$, SO_3H , SO_2R^{53a} , SR^{53} , $S(=O)R^{53a}$, $SO_2N(R^{53})_2$, $N(R^{53})_2$, $NHC(=NH)NHR^{53}$, $C(=NH)NHR^{53}$, $=NOR^{53}$, NO_2 , $C(=O)NHOR^{53}$, $C(=O)NHN(R^{53})R^{53a}$, OCH_2CO_2H , 2-(1-morpholine)ethoxy;

~~R⁵³, R^{53a}, and R⁵⁴ are each independently selected at each occurrence from the~~
~~group: hydrogen, C1-C6-alkyl, and a bond to L_n;~~

~~A_{L1} is a first ligand wherein each of the y first ligands are selected from the group~~
~~consisting of: dioxygen ligands, functionalized aminocarboxylates, halides, and combinations~~
~~thereof;~~

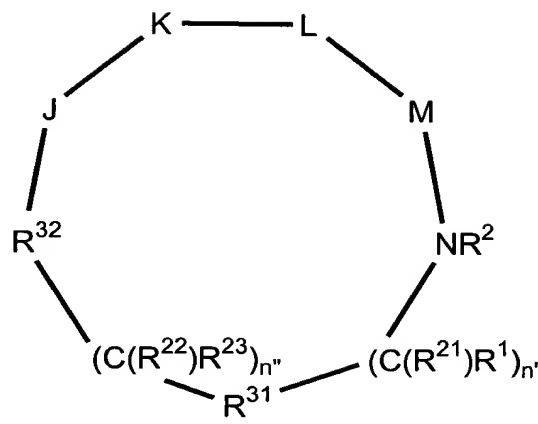
~~A_{L2} is a second ligand wherein each of the z second ligands are selected from the~~
~~group consisting of: trisubstituted phosphines, trisubstituted arsines, tetrasubstituted~~
~~diphosphines, tetrasubstituted diarsines, and combinations thereof;~~

x is independently 1-2;

y is independently 1-2; [and]

z is independently 0-4; and

wherein Q is of the formula (II),



(II)

or a pharmaceutically acceptable salt or prodrug form thereof wherein:

R³¹ is a C₆-C₁₄ aromatic carbocyclic ring system substituted with 1 R¹⁰;

R¹⁰ is -NR¹³C(=O)R¹³;

J is an L-isomer or D-isomer amino acid of structure

-N(R³)C(R⁴)(R⁵)C(=O)-, wherein:

R³ is H or C₁-C₈ alkyl;

R⁴ is H or C₁-C₃ alkyl;

R⁵ is selected from:

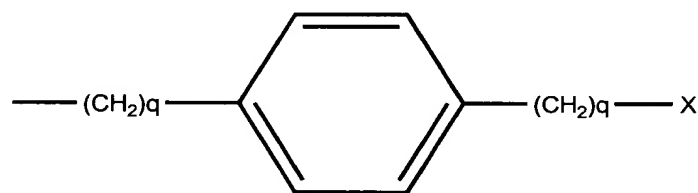
hydrogen;

C₁-C₈ alkyl substituted with 0-2 R¹¹;

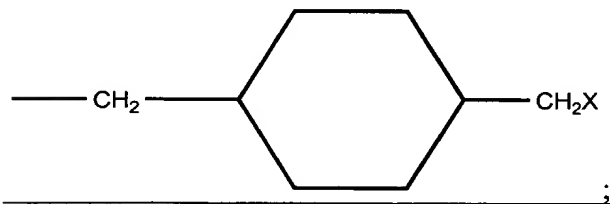
C₂-C₈ alkenyl substituted with 0-2 R¹¹;

C₂-C₈ alkynyl substituted with 0-2 R¹¹;

C₃-C₁₀ cycloalkyl substituted with 0-2 R¹¹;
aryl substituted with 0-2 R¹²;
a 5-10-membered heterocyclic ring system containing 1-4 heteroatoms independently
selected from N, S, or O, said heterocyclic ring being substituted with 0-2 R¹²;
=O, F, Cl, Br, I, -CF₃, -CN, -CO₂R¹³, -C(=O)R¹³, -C(=O)N(R¹³)₂, -CHO,
-CH₂OR¹³, -OC(=O)R¹³, -OC(=O)OR^{13a}, -OR¹³, -OC(=O)N(R¹³)₂, -NR¹³C(=O)R¹³,
-NR¹⁴C(=O)OR^{13a}, -NR¹³C(=O)N(R¹³)₂, -NR¹⁴SO₂N(R¹³)₂, -NR¹⁴SO₂R^{13a}, -SO₃H,
-SO₂R^{13a}, -SR¹³, -S(=O)R^{13a}, -SO₂N(R¹³)₂, -N(R¹³)₂, -NHC(=NH)NHR¹³,
-C(=NH)NHR¹³, =NOR¹³, NO₂, -C(=O)NHOR¹³, -C(=O)NHN(R¹³)R^{13a}, =NOR¹³,
-B(R³⁴)(R³⁵), -OCH₂CO₂H, 2-(1-morpholino)ethoxy, -SC(=NH)NHR¹³, N₃, -Si(CH₃)₃,
(C₁-C₅ alkyl)NHR¹⁶;
-(C₀-C₆ alkyl)X;



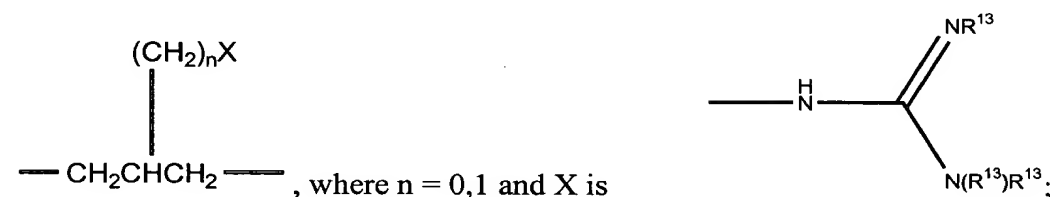
, where q is independently 0,1;



-(CH₂)_mS(O)_{p'}(CH₂)₂X, where m = 1,2 and p' = 0-2;

and

R³ and R⁴ may also be taken together to form



R³ and R⁵ can alternatively be taken together to form -(CH₂)_t- or
-CH₂S(O)_p'C(CH₃)₂-, where t = 2-4 and p' = 0-2; or

R⁴ and R⁵ can alternatively be taken together to form -(CH₂)_u-, where u = 2-5;

R¹⁶ is selected from:

an amine protecting group;

1-2 amino acids;

1-2 amino acids substituted with an amine protecting group;

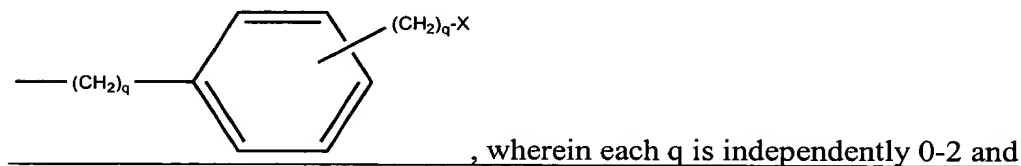
K is a D-isomer or L-isomer amino acid of structure

-N(R⁶)CH(R⁷)C(=O)-, wherein:

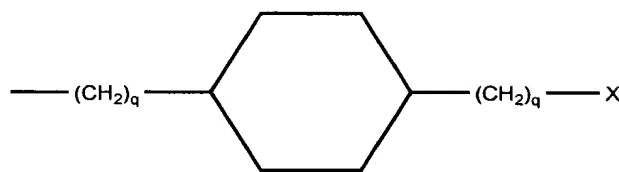
R⁶ is H or C₁-C₈ alkyl;

R⁷ is selected from:

-(C₁-C₇ alkyl)X;

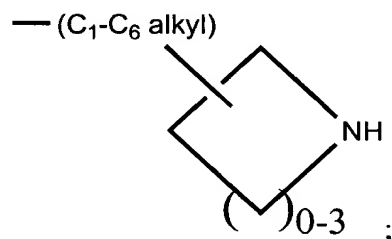


substitution on the phenyl is at the 3 or 4 position;



, wherein each q is independently 0-2

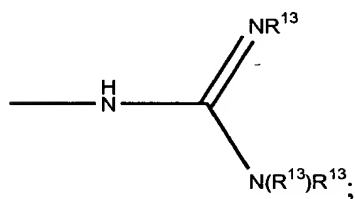
and substitution on the cyclohexyl is at the 3 or 4 position;



$-(CH_2)_mO-(C_1-C_4 \text{ alkyl})-X$, where $m = 1$ or 2 ;

$-(CH_2)_mS(O)_{p'}-(C_1-C_4 \text{ alkyl})-X$, where $m = 1$ or 2 and $p' = 0-2$; and

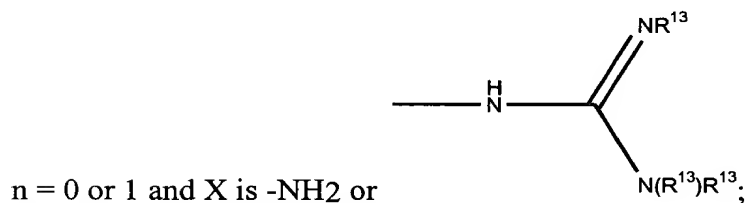
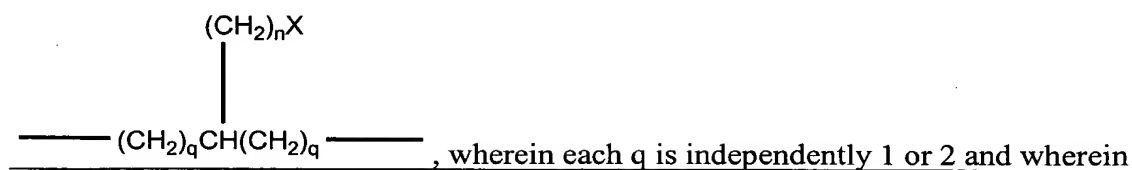
X is selected from:



$-N(R^{13})R^{13}$; $-C(=NH)(NH_2)$; $-SC(=NH)-NH_2$; $-NH-C(=NH)(NHCN)$;

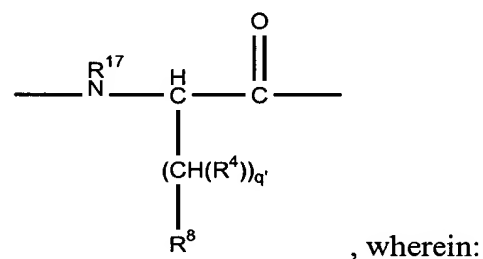
$-NH-C(=NCN)(NH_2)$; $-NH-C(=N-OR^{13})(NH_2)$;

R^6 and R^7 can alternatively be taken together to form



L is $-\text{Y}(\text{CH}_2)_v\text{C}(=\text{O})-$, wherein Y is NH and $v = 1 \text{ or } 2$;

M is a D-isomer or L-isomer amino acid of structure



q' is 0-2;

R^{17} is H, C1-C3 alkyl;

R^8 is selected from:

$-\text{CO}_2\text{R}^{13}$, $-\text{SO}_3\text{R}^{13}$, $-\text{SO}_2\text{NHR}^{14}$, $-\text{B}(\text{R}^{34})(\text{R}^{35})$, $-\text{NHSO}_2\text{CF}_3$, $-\text{CONHNHSO}_2\text{CF}_3$,
 $-\text{PO}(\text{OR}^{13})_2$, $-\text{PO}(\text{OR}^{13})\text{R}^{13}$, $-\text{SO}_2\text{NH}$ -heteroaryl (said heteroaryl being 5-10-membered
 and having 1-4 heteroatoms selected independently from N, S, or O), $-\text{SO}_2\text{NH}$ -heteroaryl
 (said heteroaryl being 5-10-membered and having 1-4 heteroatoms selected independently
 from N, S, or O), $-\text{SO}_2\text{NHCOR}^{13}$, $-\text{CONHSO}_2\text{R}^{13a}$, $-\text{CH}_2\text{CONHSO}_2\text{R}^{13a}$,

-NH₂SO₂NHCO₂R^{13a}, -NHCONHSO₂R^{13a}, -SO₂NHCONHR¹³;

R³⁴ and R³⁵ are independently selected from:

-OH,

-F,

-N(R¹³)₂, or

C₁-C₈-alkoxy;

R³⁴ and R³⁵ can alternatively be taken together to form:

a cyclic boron ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1-4 heteroatoms independently selected from N, S, or O;

a divalent cyclic boron amide where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1-4 heteroatoms independently selected from N, S, or O;

a cyclic boron amide-ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1-4 heteroatoms independently selected from N, S, or O;

R³² is -C(=O)-;

n" and n' are independently 0-2;

R¹ and R²² are independently selected from the following groups:

hydrogen,

C₁-C₈ alkyl substituted with 0-2 R¹¹;

C₂-C₈ alkenyl substituted with 0-2 R¹¹;

C2-C8 alkynyl substituted with 0-2 R¹¹;
C3-C10 cycloalkyl substituted with 0-2 R¹¹;
aryl substituted with 0-2 R¹²;
a 5-10-membered heterocyclic ring system containing 1-4 heteroatoms independently
selected from N, S, and O, said heterocyclic ring being substituted with 0-2 R¹²;
=O, F, Cl, Br, I, -CF₃, -CN, -CO₂R¹³, -C(=O)R¹³, -C(=O)N(R¹³)₂, -CHO,
-CH₂OR¹³, -OC(=O)R¹³, -OC(=O)OR^{13a}, -OR¹³, -OC(=O)N(R¹³)₂, -NR¹³C(=O)R¹³,
-NR¹⁴C(=O)OR^{13a}, -NR¹³C(=O)N(R¹³)₂, -NR¹⁴SO₂N(R¹³)₂, -NR¹⁴SO₂R^{13a}, -SO₃H,
-SO₂R^{13a}, -SR¹³, -S(=O)R^{13a}, -SO₂N(R¹³)₂, -N(R¹³)₂, -NHC(=NH)NHR¹³,
-C(=NH)NHR¹³, =NOR¹³, NO₂, -C(=O)NHOR¹³, -C(=O)NHN(R¹³)R^{13a}, -OCH₂CO₂H,
2-(1-morpholino)ethoxy;

R¹ and R²¹ can alternatively join to form a 3-7 membered carbocyclic ring
substituted with 0-2 R¹²;

when n' is 2, R¹ or R²¹ can alternatively be taken together with R¹ or R²¹ on an
adjacent carbon atom to form a direct bond, thereby to form a double or triple bond between
said carbon atoms;

R²² and R²³ can alternatively join to form a 3-7 membered carbocyclic ring
substituted with 0-2 R¹²;

when n" is 2, R²² or R²³ can alternatively be taken together with R²² or R²³ on an adjacent carbon atom to form a direct bond, thereby to form a double or triple bond between the adjacent carbon atoms;

R¹ and R², where R²¹ is H, can alternatively join to form a 5-8 membered carbocyclic ring substituted with 0-2 R¹²;

R¹¹ is selected from one or more of the following:

=O, F, Cl, Br, I, -CF₃, -CN, -CO₂R¹³, -C(=O)R¹³, -C(=O)N(R¹³)₂, -CHO, -CH₂OR¹³, -OC(=O)R¹³, -OC(=O)OR^{13a}, -OR¹³, -OC(=O)N(R¹³)₂, -NR¹³C(=O)R¹³, -NR¹⁴C(=O)OR^{13a}, -NR¹³C(=O)N(R¹³)₂, -NR¹⁴SO₂N(R¹³)₂, -NR¹⁴SO₂R^{13a}, -SO₃H, -SO₂R^{13a}, -SR¹³, -S(=O)R^{13a}, -SO₂N(R¹³)₂, -N(R¹³)₂, -NHC(=NH)NHR¹³, -C(=NH)NHR¹³, =NOR¹³, NO₂, -C(=O)NHOR¹³, -C(=O)NHN(R¹³)R^{13a}, -OCH₂CO₂H, 2-(1-morpholino)ethoxy,

C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆ alkoxyalkyl, C₃-C₆ cycloalkoxy, C₁-C₄ alkyl (alkyl being substituted with 1-5 groups selected independently from: -NR¹³R¹⁴, -CF₃, NO₂, -SO₂R^{13a}, or -S(=O)R^{13a}),

aryl substituted with 0-2 R¹²,

a 5-10-membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, said heterocyclic ring being substituted with 0-2 R¹²;

R¹² is selected from one or more of the following:

phenyl, benzyl, phenethyl, phenoxy, benzyloxy, halogen, hydroxy, nitro, cyano,
C₁-C₅ alkyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkylmethyl, C₇-C₁₀ arylalkyl, C₁-C₅ alkoxy,
-CO₂R¹³, -C(=O)NHOR^{13a}, -C(=O)NHN(R¹³)₂, =NOR¹³, -B(R³⁴)(R³⁵), C₃-C₆
cycloalkoxy, -OC(=O)R¹³, -C(=O)R¹³, -OC(=O)OR^{13a}, -OR¹³, -(C₁-C₄ alkyl)-OR¹³,
-N(R¹³)₂, -OC(=O)N(R¹³)₂, -NR¹³C(=O)R¹³, -NR¹³C(=O)OR^{13a}, -NR¹³C(=O)N(R¹³)₂,
-NR¹³SO₂N(R¹³)₂, -NR¹³SO₂R^{13a}, -SO₃H, -SO₂R^{13a}, -S(=O)R^{13a}, -SR¹³,
-SO₂N(R¹³)₂, C₂-C₆ alkoxyalkyl, methylenedioxy, ethylenedioxy, C₁-C₄ haloalkyl, C₁-C₄
haloalkoxy, C₁-C₄ alkylcarbonyloxy, C₁-C₄ alkylcarbonyl, C₁-C₄ alkylcarbonylamino,
-OCH₂CO₂H, 2-(1-morpholino)ethoxy, C₁-C₄ alkyl (alkyl being substituted with -N(R¹³)₂,
-CF₃, NO₂, or -S(=O)R^{13a});

R¹³ is selected independently from: H, C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₄-C₁₂
alkylcycloalkyl, aryl, -(C₁-C₁₀ alkyl)aryl, or C₃-C₁₀ alkoxyalkyl;

R^{13a} is C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₄-C₁₂ alkylcycloalkyl, aryl, -(C₁-C₁₀
alkyl)aryl, or C₃-C₁₀ alkoxyalkyl;

when two R¹³ groups are bonded to a single N, said R¹³ groups may alternatively be
taken together to form -(CH₂)₂₋₅- or -(CH₂)O(CH₂)-;

R¹⁴ is OH, H, C₁-C₄ alkyl, or benzyl;

R²¹ and R²³ are independently selected from:

hydrogen;

C₁-C₄ alkyl, optionally substituted with 1-6 halogen; and

benzyl; and

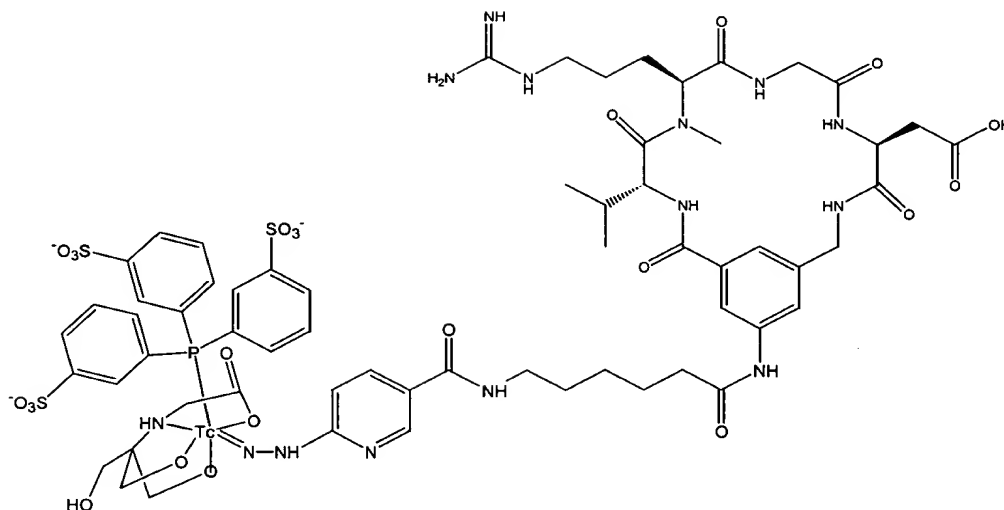
R² is H or C₁-C₈ alkyl.

21. (previously added) The method of Claim 20 wherein M_T is selected from the group consisting of: technetium-99m, rhenium-186, and rhenium-188.

22. (canceled)

23. (canceled)

24. (previously added) The method of Claim 20 wherein the localization step comprises the step of localizing a compound of the formula (IV) at the pulmonary embolus:



(IV).

25. (canceled)

26. (canceled)

27. (currently amended) The method of Claim [[26]] 20 wherein the acquisition step comprises the step of acquiring single photon emission computed tomography images of the pulmonary embolus.

28. (currently amended) The method of Claim [[17]] 20 wherein the acquisition step comprises the step of acquiring transaxial image slices and further comprising the step of reformatting the transaxial image slices into image slices that are parallel to a long axis associated with the pulmonary embolus.

29. (currently amended) The method of Claim [[17]] 20 comprising the step of displaying the two dimensional array as a reprojected image.

30. (currently amended) The method of Claim [[17]] 20 wherein the scanning step is performed at a series of angles.

31. (previously added) The method of Claim 30 wherein the assignment step is

performed at each of the series of angles.

32. (previously added) The method of Claim 31 comprising the step of sequentially displaying the two-dimensional arrays as reprojected images.

33-54. (canceled)

55. (previously added) The method of Claim 20 comprising the step of displaying the two-dimensional array as a reprojected image.

56. (previously added) The method of Claim 20 wherein the scanning step is performed at a series of angles.

57. (previously added) The method of Claim 56 wherein the assignment step is performed at each of the series of angles.

58. (previously added) The method of Claim 57 comprising the step of sequentially displaying the two-dimensional arrays as reprojected images.